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Diabetes in South Asians: Is the Phenotype Different?

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The South Asian region is home to more than 20% of the world's population and includes three of the ten most populous countries in the world. Significant numbers of South Asians (SA) also live in North America, the Caribbean, Europe, the U.K., the Middle East, southern Africa, and the Pacific region.

South Asia forms one of the epicenters of the global diabetes epidemic. According to estimates released by the International Diabetes Federation, more than 70 million individuals in the region have diabetes (1). Over the past couple of decades, there has been a worrying increase in the prevalence rates of diabetes in the region. The earliest multicenter studies on the prevalence of diabetes in India in the early 1970s showed rates of around 2% in urban areas and 1% in rural areas (2). The latest available data show that these rates have increased to nearly 20% in some urban areas and 10% in the rural areas (3).

Studies in the South Asian diaspora residing in the U.K. during the early 1980s suggested the possibility of an Asian Indian or South Asian phenotype (Fig. 1). This term refers to a combination of characteristics that predisposes SA to the development of insulin resistance, type 2 diabetes, and cardiovascular disease. It has also been shown that type 2 diabetes occurs at younger ages and at lower levels of BMI in SA compared with Caucasians (4). In spite of a relatively lower rate of obesity as defined by BMI cut points, SA tend to have larger waist measurements and waist-to-hip ratios, indicating a greater degree of central body obesity (5). This is associated with a characteristic metabolic profile with higher insulin levels (6), a greater degree of insulin resistance (7), and a higher prevalence of diabetes (8). Insulin resistance has been demonstrated in Asian Indians even during adolescence (9). Hyperinsulinemia—a corollary of insulin resistance—seems to be present among SA even at birth, as evidenced by studies in cord blood (10).

The pathogenesis of insulin resistance in SA has been a matter of much discussion. In this issue, Bakker et al. (11) explore the possibility that SA have impaired mitochondrial fatty acid oxidation in skeletal muscle and adipose tissue, leading to increased intramyocyte deposition of fat and consequent development of insulin resistance. To this end, they administered a high-fat, high-calorie (HFHC) diet to 12 healthy, young, lean, male SA and 12 matched Caucasians for 5 days. Insulin resistance was assessed before and after the diet using a hyperinsulinemic-euglycemic clamp, and skeletal muscle biopsies and indirect calorimetry were performed before and after the diet. Their results show that the 5-day HFHC diet reduced insulin-stimulated glucose disposal rate in SA but not in Caucasians, indicating the rapid induction of insulin resistance in the former group. Interestingly, there was no difference in the baseline fasting insulin levels or peripheral insulin sensitivity between the two groups, probably due to the fact that the subjects in each arm were young and lean with no excess visceral adiposity. Even so, following the clamp, insulin levels rose only in SA, indicating lower levels of insulin sensitivity in this group.

The current study has focused on two possible mechanistic explanations for the impairment of insulin sensitivity following an HFHC diet. First, impaired nonoxidative glucose disposal (NOGD) has been identified as one of the main defects in type 2 diabetes (12). While SA had higher levels of NOGD at baseline, this was achieved only at the expense of higher insulin levels. Following the study diet, NOGD decreased significantly only in SA. However, no significant differences were found in the proteins and genes involved in glycogen synthesis among the two groups. Explanation of the mechanism of impaired NOGD among SA would form an interesting topic for further research.

The second mechanism studied by the authors focuses on the nutrient-sensing mammalian target of rapamycin (mTOR) pathway, activation of which could conceivably impair mitochondrial beta oxidation of fatty acids and

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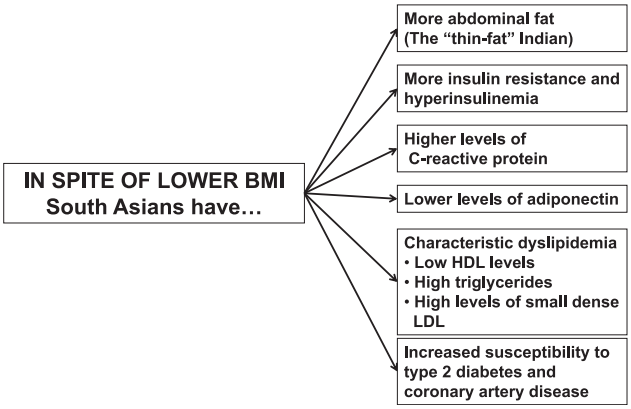

Figure 1—The South Asian ("Asian Indian") phenotype.

lead to ectopic deposition of fat in the peripheral tissues. However, no differences were found among the two groups with respect to activity of the mTOR pathway, probably on account of the small sample size as well as relative youth and leanness of the study subjects. A recent study comparing mitochondrial oxidative phosphorylative (OXPHOS) capacity between Asian Indians and North American Caucasians showed that the former group had higher OXPHOS capacity in spite of being more insulin-resistant, suggesting that mitochondrial dysfunction may not play a major role in the pathogenesis of insulin resistance in this population (13).

The avid response of SA to an HFHC diet has important implications. The diet of native Asian Indians has undergone a sea change over the last three decades. Consequent to rapid economic development, individuals in these countries, particularly those in the younger age-group, have higher levels of disposable income than ever before. Simultaneously, the climate of economic liberalization and globalization prevailing in many of these countries has led to the easy availability of high-calorie, high-carbohydrate (refined), high-fat food choices, which have found wide acceptance among the population, particularly in the urban areas (14). Over the past two decades, the total daily intake of fat has increased by 7 g in the rural areas and 6 g in the urban areas of India (15). Even so, fat still contributes less than 15% to the total calories of the average Indian diet (16); it is more likely that the high intake of refined carbohydrates (e.g., polished white rice or other refined cereals) and the consequent high glycemic load is contributing to the increased insulin resistance and type 2 diabetes and metabolic syndrome in this population (17–19).

In conclusion, the study by Bakker et al. (11) throws light on a possible mechanism by which the increased propensity of SA to type 2 diabetes could be explained. Although the study has not given any mechanistic explanations, the results do suggest that SA tend to adapt adversely to a "Western" dietary pattern. The results also suggest a possible means by which the epidemic of type 2 diabetes in South Asia can be curtailed. Raising awareness among the population regarding the deleterious effects of a high-fat, high-carbohydrate, high-calorie diet and encouraging them to continue the more healthy traditional foods could help individuals make healthy dietary choices, helping to reduce the risk of not only type 2 diabetes but of cardiovascular disease as well.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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